

Amendments to the Specification:

Please amend the specification as follows:

Please delete paragraph on page 41, line 29 and replace with the following paragraph:

FIG. **1a-b** ~~shows~~ **show** the PTP20 nucleic acid sequence isolated from Rat-1 cells and the corresponding amino acid sequence encoded by this nucleic acid molecule (**SEQ ID NOS 31 & 32 respectively**).

Please delete paragraph on page 41, line 32 and replace with the following paragraph:

FIG. **2a-f** ~~shows~~ **show** the nucleotide sequence and predicted amino acid sequence of PCP-2 (**SEQ ID NOS 33 & 34 respectively**). PCP-2 nucleotide sequence (5581 bp) and deduced amino acid sequence (1430 amino acid). The predicted initiating methionine (Kozak, 1984) and putative signal peptide (von Heijne, 1986) are indicated by thin single underlining. The transmembrane domain is indicated by thick underlining. The two tandem phosphatase domains are boxed. The MAM domain is indicated by a shaded box, the Ig-like domain is shown in bold italic characters, and the four fibronectin type III-like domains are indicated by dotted underlining. The polyadenylation motif (AATAAA) is shown in bold characters.

Please delete paragraph on page 42, line 6 and replace with the following paragraph:

FIG. **3a-d** ~~shows~~ **show** the nucleotide sequence of human BDP1 cDNA clone and introns (**SEQ ID NOS 35 & 36 respectively**). The sequence first identified by PCR cloning is bordered by arrow heads. A GC-rich track which is part of the Kozak sequence (Kozak, 1987) is indicated by a dotted line. T-rich and the AATAAA sequences required for polyadenylation are underlined. **As diagrammed on page 3/15 of the figures, figure 3a should be viewed adjacent to figure 3b and figure 3c should be viewed adjacent to figure 3d.**

Please delete paragraph on page 42, line 12 and replace with the following paragraph:

FIG. 4 compares amino acid sequences **(SEQ ID NOS 5, 39, 40 & 41 respectively)** encoded by mCLK1, mCLK2, mCLK3, and mCLK4 nucleic acid molecules cloned from mouse cells. Each amino acid sequence is encoded between a start codon and a stop codon from its respective nucleic acid molecule. Dots indicate identical amino acids and hyphens are introduced for optimal alignment. The predicted nuclear localization signals are underlined. Invariant amino acids signifying CDC2 like kinases are printed in bold. The catalytic domain is indicated by arrows. The LAMMER signature is indicated by asterisks.

Please delete paragraph on page 42, line 23 and replace with the following paragraph:

FIG. 5 shows the deduced amino acid sequences of SIRP4 and SIRP1 **(SEQ ID NOS 37 & 38 respectively)**. Identical amino acids are boxed. The putative signal sequence and transmembrane region are indicated by thin and thick overlines, respectively. Three Ig-like domains are indicated by stippled overlines. Potential tyrosine phosphorylation sites are shown in bold, the C-terminal proline rich region is shaded. The location of oligonucleotides flanking the Ex region is indicated by stars.

Please delete paragraph on page 70, line 18 and replace with the following paragraph:

The degenerate primers used to identify PTP20 were FWXMXW **(SEQ ID NO: 1)** (sense) and HCSAG(S/I/V)G **(SEQ ID NO: 2)** (antisense). Random-primed cDNA (up to 50 ng) from PC12 cell RNA was used as a template. Both sense and antisense primers were added to a 100 ml reaction mixture containing 20 mM Tris-HCl (pH 8.4), 50 mM-KCl, 2.5 mM MgCl₂, 0.01% BSA, all four dNTPs (each at 200 mM), 1 unit of Taq polymerase (Boehringer Mannheim) and template cDNA. Thirty-five cycles were carried out on a thermal cycler; each cycle involved incubation at 94°C for 1 min, at 42°C for 1 min and 72°C for 1 min. The PCR products were separated on a 1.5% agarose gel. Fragments of 350-400 bp were excised, subcloned and sequenced.

Please delete paragraph on page 71, line 15 and replace with the following paragraph:

We used sequence homology and PCR amplification to clone the protein tyrosine phosphatases expressed in human brain tissue. The degenerate primers for PCR were designed according to the consensus sequences from alignment of amino acid sequences of known PTPases. The longest consensus sequences FWXMXW (**SEQ ID NO: 1**) and HCSAGXG (**SEQ ID NO: 2**) in catalytic domains were selected. A single-lane sequencing of 379 amplified CDNA clones identified 15 different CDNA clones, including CD45, LAR, MEG1, PTPase, PTPase, PTPase, PTPase, PTPase, PTPase and PTPase 1D. One clone encoded a novel putative protein tyrosine phosphatase. We called the clone BDP1 because it was found in human brain cDNA.

Please delete paragraph on page 72, line 17 and replace with the following paragraph:

The degenerate primers used to identify BDP1 were FWXMXW (**SEQ ID NO: 1**) (sense) and HCSAG(S/I/V)G (**SEQ ID NO: 2**) (antisense). 2 µg of human brain poly(A)+RNA were used for the synthesis of the first-strand cDNA, employing oligo(dT)-priming and RNase H-negative reverse transcriptase (GIBCO/BRL). 50 ng of synthesized cDNA were amplified with 30 pmol of each degenerate primer in 100 µl of PCR solution for 30 cycles. Amplified PCR-products were digested with BamHI or EcoRI and separated on 6% acrylamide gel. Fragments of about 350 bp were excised, subcloned and sequenced.

Please delete paragraph on page 74, line 12 and replace with the following paragraph:

The deduced amino acid sequence from aa 1 to 25 at the N-terminus was compared with sequences in data banks. It was found that the 70 KDa cyclase-associated CAP protein of yeast (Field, et al. (1990) Cell 61, 319-327), rat (Selicof, et al. (1993) J. Biol. Chem. 268, 13448-13453) and human (Matviw, et al (1992) Mol. Cell. Biol. 12, 5033-5040) were homologous, as is illustrated in FIG. 2B. Especially the FLERLE (**SEQ ID NO:3**) sequence could also be found in the acidic FGF molecule near the second Cys consensus residue, and was also reported to take part in the binding to its own receptor molecule on the cell surface (Thomas, et al. (1991). Ann. New York. Acad. Sci. 9-17).

Please delete paragraph on page 76, line 9 and replace with the following paragraph:

PCR reactions were performed using degenerate oligonucleotide primers corresponding to the consensus sequences RXXMXW (**SEQ ID NO: 4**) and HCSAG (S/I/V) G (**SEQ ID NO: 2**), and the GeneAmp.RTM. kit (Perkin-Elmer/Cetus) and pool of poly (A)+RNA from 9 human pancreatic carcinoma cell lines: A590, A818-7, AsPc 1, BxPC-2, Capan-1, Capan-2, Colo357, DAN-G and SW850 (ATCC, Rockville, Md.). The PCR fragments were isolated, subcloned, and sequenced.

Please delete paragraph on page 80, line 3 and replace with the following paragraph:

The PTP20 mutant containing a cysteine to serine alteration at position 229 was generated using a oligonucleotide primer, CTCTGTGTCCACAGCAGTGCTGGCTGT (**SEQ ID NO: 6**). Kunkel, PNAS 82:488, 1985.) The mutation was confirmed by DNA sequencing.

Please delete paragraph on page 88, line 6 and replace with the following paragraph:

The signature sequences HRDLAAR (**SEQ ID NO: 7**) in the catalytic subdomain VI and D(V/M)WS(Y/F)G (**SEQ ID NO: 8**) in subdomain IX were used to create degenerate oligonucleotides. (Ciossek et al., Oncogene 11:2085, 1995.) Reverse transcriptase PCR reactions were performed with 2 µg of total RNA prepared from confluent or differentiated (day 7) mouse C2C12 myoblasts (Lechner et al., PNAS 93:4355, 1996). (Ciossek et al., Oncogene 11:2085, 1995.) Briefly, 2 µg of RNA were reverse transcribed in the presence of 1 µM degenerate antisense primer, 250 µM of each nucleotide and 75 units of Stratascript reverse transcriptase (Stratagene) in a total volume of 20 µl for 30 min at 42°C 2 µl of the above reaction was used in a PCR reaction using degenerate sense and antisense oligonucleotides (1 µM each), 25 µM of each nucleotide and 2.5 units Taq polymerase (Boehringer). 30 cycles were performed with 1 min for each 94°C, 50°C and 72°C step. Fragments of approximately 250 bp were gel purified, cloned in Bluescript and sequenced.

Please delete paragraph on page 88, line 24 and replace with the following paragraph:

mCLK2, mCLK3 and mCLK4 were cloned from a mouse embryo 11.5 p.c. 1ZAP cDNA library (Ciossek et al., supra) using the isolated PCR fragment as a probe according to manufacturer's instructions (final wash in 0.5X SSC/0.1% SDS at 42°C) (Stratagene). mCLK1 was cloned by reverse transcriptase PCR from 1 µg brain poly (A)⁺ RNA using specific primers mCLK1s-Bam, CGGGATCCCTTCGCCTTGCAGCTTTGTC (**SEQ ID NO: 9**) and mCLK1as-EcoRI, CGGAATTCCTAGACTGATACAGTCTGTAAG (**SEQ ID NO: 10**), and Pwo polymerase (Doehringer).

Please delete paragraph on page 88, line 33 and replace with the following paragraph:

From the approximately 300 fragments which were sequenced from the first PCR reaction, one was novel. It resembled a member of the LAMMER family of dual specificity kinases (Yun et al., Genes. Dev. 8:1160, 1994), also known as CLK kinases (Ben-David et al., EMBO J. 10:317, 1991) or STY (Howell et al., Mol. Cell. Biol. 11:568, 1991) and shared a high homology to a part of the human cDNA hCLK2. Full length clones of this and three related proteins were obtained from a mouse embryonic cDNA library as described. The same libraries were rescreened with a mixture of mCLK1, 2, 3, and 4 fragments at low stringency to isolate additional novel members of this family. Reverse transcriptase PCR reactions were performed on brain, kidney and liver poly (A)⁺ RNA with degenerate primers coding for the DLKPEN (**SEQ ID NO: 11**) and AMMERI (**SEQ ID NO: 12**) motifs. These efforts did not identify additional genes.

Please delete paragraph on page 90, line 30 and replace with the following paragraph:

GST fusion constructs were generated by subcloning full length mCLK1, mCLK2, mCLK3 and mCLK4 cDNAs by PCR into pGEX vectors (Pharmacia), creating in-frame glutathione S-transferase (GST) fusion constructs using the-following primers for PCR: mCLK1s-Bam (as above); mCLK1as-Not I, TATAGCGGCCGCTAGACTGATACAGTCTGT (**SEQ ID NO: 13**); mCLK2s-Sma I, TCCCCCGGGATGCCCCATCCCCGAAGG- TACCA (**SEQ ID NO: 14**); mCLK2as-Not I,

TATAGCGGCCGCTCACCGACTGATATCCCGACTGGAGTC (**SEQ ID NO: 15**); mCLK3s-Sma I, TCCCCCGGGGAGACGATGCATCACTGTAAG (**SEQ ID NO: 16**); mCLK3as-Not I, TATAGCGGCCGCGCTGGCCTGCACCTGTCATCTGCTGGG (**SEQ ID NO: 17**); mCLK4s-EcoRI, CGGAATTCATGCGGCATTCCAAACGAACTC (**SEQ ID NO: 18**); mCLK4as-Not I, TATAGCGGCCGCCCCTGACTCCCACTCATTTCTTTTAA (**SEQ ID NO: 19**). The cDNAs encoding the fusion construct were then recloned in pcDNA3 (Invitrogen) by PCR using the GST upstream primers: GST-EcoRI, CGGAATTCCGCCACCATGGCCCCTATACTAGGTTAT (**SEQ ID NO: 20**) (for mCLK1) and GST-Hind III, GCCAAGCTTGCCACCATGGCCCCTATACTA- GGTTAT (**SEQ ID NO: 21**) (for mCLK2, mCLK3 and mCLK4).

Please delete paragraph on page 91, line 9 and replace with the following paragraph:

Integrity of the clones was checked by sequencing and by a coupled transcription-translation assay using T7 RNA polymerase and rabbit reticulocyte lysate according to the manufacturer's protocol (Promega). mCLK 1-4 mutants containing a lysine (K) to arginine (R) substitution at position 190 (mCLK1), 192 (mCLK2), 186 (mCLK3) and 189 (mCLK4) were generated using a site-directed mutagenesis protocol. (Kunkel, PNAS 82:488-, 1985.) Oligonucleotide primers were as follows: (mCLK1-K190R) GTAGCAGTAAGAATAGTTAAA (**SEQ ID NO: 22**); (mCLK2-K192R) GTTGCCCTGAGGATCATTAAGAAT (**SEQ ID NO: 23**); (mCLK3-K186R) GTTGCCCTGAGGATCATCCGGAAT (**SEQ ID NO: 24**); (mCLK4-K189R) TACAATTCTCACTGCTACATGTAAGCCATC (**SEQ ID NO: 25**).

Please delete paragraph on page 96, line 27 and replace with the following paragraph:

Insulin treated Rat1-IR were used to purify the 110 kDa SHP-2 binding glycoprotein using standard chromatography procedures. Approximately 4 mg of the glycoprotein that copurified with SHP-2 were obtained and subject to microsequence analysis. This yielded five peptide sequences: PIYSFIGGEHFPR (**SEQ ID NO: 26**), IVEPDTEIK (**SEQ ID NO: 27**), YGFSPR (**SEQ ID NO: 28**), IKEVAHVNLVR (**SEQ ID NO: 29**), VAAGDSAT (**SEQ ID NO: 30**). Computer aided search in the EST database led to the identification of a

305 bp rat sequence (accession Nr.: H31804) and subsequent human cDNA fragment of 2 kb (EMBL databank, accession Nr.: U6701) containing matching and homologous sequences, respectively.